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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/572,523

01/19/2007

Shabtai Bauer

2488.036

4723

23405

7590

02/18/2010

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EXAMINER

GEBREYESUS, KAGNEW H

ART UNIT

PAPER NUMBER

1656

MAIL DATE

DELIVERY MODE

02/18/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/572,523	Applicant(s) BAUER, SHABTAI	
	Examiner KAGNEW H. GEBREYESUS	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 25-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>3/21/2006, 11/07/2006, 2/09/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's election dated November 2, 2009 in reply to restriction requirements mailed on October 6, 2009 is acknowledged. Applicants have elected Group 1 comprising claims 1-24. Claims 25-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected groups, there being no allowable or linking claims.

Applicants further state that due to the difference in the process taught by Lebing et al and their process, the product produced is also patentably distinct such that all the claims should be rejoined if the process is found allowable. However it is to be noted by the applicant that, only if applicant elects claims directed to the product, and said product claim is subsequently found allowable, that withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04.

Thus the restriction requirement is made final. Claims 1-24 are present for examination.

Priority

Priority for this application is acknowledged for benefit of PCT/IL/04/00881 filed on September 22, 2004 which further claims priority from U.S. Provisional Application 60/503902 filed on September 22, 2003.

Information Disclosure Statement

The information disclosure statement filed on 3/21/06, 11/07/06 and 2/09/07 for which a copy of the patent publication has been submitted in this application has been considered as shown by the Examiners signature.

Oath/Declaration

The oath or declaration submitted on 1/19/07 has been reviewed and is in compliance with 37 CFR 1.56.

Drawings

The drawings were received on March 21, 2006. These drawings are accepted.

Specification

The specification is objected to because the first line of the specification does not contain the continuity data with regard to PCT/IL/04/00881 filed September 22, 2010 which further claims priority from provisional application 60/503902.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

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3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6462180 (Lebing et al¹) further in view of US 5,610,285 (Lebing et al²). Lebing et al¹ teach a method of purification of α -1 proteinase inhibitor (α -1API) from aqueous solutions, such as human plasma or Cohn fraction IV-1, by precipitating contaminating proteins and lipids (see column 4, line 24-25) from the aqueous solution, followed by dilution of the solution to adjust its conductivity, and passing of the solution through an anion exchange resin such as TMAE or DEAE-Sepharose whereby the eluent from the anion exchange is submitted to a purification step comprising cation exchange chromatography. Likewise US 5,610,285 (Lebing et al²) in example 1 teach a stepwise purification Cohn fraction IV-1 comprising the steps of – an anion exchange using DEAE which binds the α -1 proteinase inhibitor (α -1API). The column was washed and then the α -1API fraction was eluted. The eluent was adjusted to pH to 5.45 and loaded on a cation resin, the flow through from the cation exchange containing the α -1API submitted to a viral inactivation step comprising viral inactivation and viral exclusion/filtration, solvent detergent treatment for viral inactivation. The virally inactivated solution was diafiltered and the solution was adjusted to pH to 5.45 and loaded on a second cation resin to remove any remaining contaminant of the α -1API. US 5,610,285 (Lebing et al²)'s method yielded 95% purity for a final product. Furthermore methods of removing lipids using silicon dioxide (also

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called Aerosil as seen in applicant's specification page 28 line 12) was known in the art. For example US 6,093,324 (Bertolini et al) teach use of various formulation Aerosil as effective colloidal silica preparations for removing lipids for the purification of IgG from Cohn fractions. Thus it would have been obvious to use available delipidating agents such as Aerosil to remove lipids in the preparation of α -1API.

Lebing et al¹ also teach that their purification method can achieve a purity of up to 98% (see column 3, line 57-58) (obvious over claims 1-7). Lebing et al's teaches that human plasma or Cohn fraction IV-1 can be sources of α -1API and teaches that the procedure further includes a virus removal step(s) such as nanofiltration and/or inactivation using a non-ionic detergent such as Tween 20 (obvious over claims 8-14).

Furthermore Lebing et al¹ also teach that a portion of contaminating proteins is removed from the aqueous solution, so that a partially purified solution containing α -1API is obtained by for example, precipitating with polyethylene glycol (PEG) to the aqueous solution and adjusting the pH of the solution to from about 5.0 to about 6.0 (obvious over claims 16-19). Furthermore claim 16 teaches adjusting the pH 6.25-7.25 of the purified solution (1st step), prior to passing the solution containing α -1API through the anion exchange resin (thus obvious over the principle used in claim 21).

Following the filtration, the resulting solution containing purified α -1API is concentrated by ultrafiltration and diafiltration. After diafiltration, the concentrated α -1API is formulated at about 55 mg/ml of 20 mM NaPO₄ and 100 mM NaCl at pH 7.0. The formulated solution is sterile filtered (obvious over claims 22-24).

Both Lebing et al^{1,2} do not teach a third step wherein the eluent from the cation exchange step is submitted to an anion exchange step.

However it would have been obvious to a person of ordinary skill in the art motivated to further to further add an additional step of an anion or a cation exchange chromatography step in order to further optimize the purity obtained because α -1API is used to treat human diseases such as congenital emphysema (see for example Chen et al attached) . This is further evidenced by US 5,610,285 Lebing et al² who teach a purification method wherein Cohn fraction IV in suspension is submitted to the sequential steps of anion exchange, cation exchange viral inactivation, a second cation exchange and the flow through is sterile filtered.

Therefore, given the disclosures of US 6462180 (Lebing et al¹) further in view of US 5,610,285 (Lebing et al²), and the overall knowledge in the art (such as for example the knowledge that proteins can carry both negatively and positively charged groups and that the net charge of the protein is dependent on pH, and that no binding to any type of ion-exchange gel matrix will occur at the isoelectric point (pI), since the net charge of a protein is zero), it would have been obvious for a person of ordinary skilled in the art in protein purification to optimize the procedures by modifying the steps such that an additional step of anion exchange with the pH and salt concentration within the parameters disclosed in Lebing et al^{1,2} (which would also be conventional working conditions), because they are deemed merely a matter of judicious selection and routine optimization well within the purview of the skilled artisan.

Furthermore, selecting the type and/or sequence of ion exchange resins used can be routinely optimized by one of ordinary skill in the art of practicing the invention disclosed by the references. (Please note the selection of any order of performing process steps is *prima facie*

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obvious in the absence of new or unexpected results. (see, e.g., *Ex parte Rubin*, 128 USPQ 440, 1959, and *In re Burhans*, 154 F.2d 690, 69 USPQ 330-CCPA 1946) MPEP 2144.04.

Accordingly, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Conclusion: No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus/
Examiner, Art Unit 1656

/Manjunath N. Rao /
Supervisory Patent Examiner, Art Unit 1656